REMARKS

Claims 33 through 44 are pending in the instant application.

Claims 39 and 44 have been withdrawn from consideration by the Examiner as being drawn to nonelected subject matter.

Claims 33-38 and 40-43 have been rejected. Claims 33 and 40 have been objected to. Claims 33, 36 and 40 have been amended. Claims 42 and 43 have been canceled. Support for these amendments is provided in Claim 5 of the original application, claims 42 and 43, now canceled, and page 2, page 24 and Example 4 of the specification

Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Withdrawal of Claims 39 and 44

Claims 39 and 44 have been withdrawn as not reading on the elected species. It is respectfully requested that these claims be rejoined upon allowance of the generic claims in accordance with MPEP § 809.01 and 37 C.F.R. § 1.146.

I. Objection to Claim 33 and 40

Claim 33 and claim 40 have been objected to.

Claim 33 has been amended as suggested by the Examiner to correct the term "Transforming growth factor-β induced

gene-h3". Support for this amendment is provided at page 2, line 23 of the specification.

Claim 40 has been amended as suggested by the Examiner to clarify the relationship between the antibody and the protein.

Withdrawal of these objections is therefore respectfully requested.

II. Rejection of Claims 36-38 under 35 U.S.C. 112, first paragraph - Written Description

Claims 36-38 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner suggests that step (a) reciting recombinant protein being reacted with the urine sample introduces new matter because the specification and original claim 5 teaches reaction of the sample with an antibody against the protein.

Accordingly, Applicants have amended step (a) of claim 36 to state reacting an antibody against a recombinant protein of βig-h3 or βig-h3 fasciclin-1 (fas-1) domain with the urine sample. Support for this amendment is provided in original claim 5 and in Example 4 of the specification.

Withdrawal of this rejection is respectfully requested in light of this amendment.

III. Rejection of Claims 33-38 and 40-43 under 35 U.S.C. 112, first paragraph - Lack of Enablement

Claims 33-38 and 40-43 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Applicants respectfully traverse this rejection.

Arguments presented by Applicants in the last response were deemed unpersuasive as the Examiner suggests that while the data of Table 1 shows a clear separation between βig-h3 levels in Type II diabetes vs. normal subjects, it would appear with respect to the population of diabetic vs. diabetic with renal disease that the separation is not statistically significant. Thus, the Examiner suggests that these data indicate that βig-h3 is specifically elevated in Type II diabetes, but do not necessarily indicate that βig-h3 is a marker that is specific to kidney damage, since it was apparently elevated in all diabetic subjects regardless of whether they had kidney damage or not.

MPEP 2164.01(a) is clear; any conclusion of nonenablement must be based on the evidence as a whole.

As already pointed out by Applicants in the response filed February 20, 2007, in addition to data presented in Table I, the utility of measuring βig-h3 levels in urine as

an indicator of damage to the kidney at an early stage was confirmed in a diabetic animal model (See Example 4-2). As shown therein, while blood urea and creatinine were normal and kidney tissues seemed normal in the diabetic animal model at day 5, the βig-h3 concentration was increased on average by 4-fold 5 days after inducing diabetes (see FIG. 13 and 14). This measurable increase of βig-h3 levels in urine on the fifth day is indicative of early damage to the kidneys, which could not be detected by the traditional test methods.

MPEP 2164.02 is clear; when a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating to a specific condition, unless the Examiner has evidence that the model does not correlate. The Examiner has provided no evidence that data from the animal model showing a measurable increase of βig-h3 levels in urine on the fifth day is not indicative of early damage to the kidneys which could not be detected by the traditional test methods. Accordingly, consideration of this evidence confirming the utility of measuring βig-h3 levels in urine as an indicator of damage to the kidney at an early stage is respectfully requested.

Applicants also respectfully direct the Examiner to teachings in the specification in Example 4 at pages 38-45

wherein various experiments measuring βig-h3 levels in urine indicative of renal damage are set forth. Such experiments clearly provide guidance for one of skill in the art to select "cut-off" values without any undue burden.

Finally, it is respectfully pointed out that the Examiner's concern regarding the possibility of false positives is improper. MPEP 2164 and the case law are clear; to comply with 35 U.S.C. 112, first paragraph, it is not necessary to "enable one of ordinary skill in the art to make and use a perfected, commercially viable embodiment absent a claim limitation to that effect." Instead, what is required is that the information contained in the disclosure be sufficient to inform those skilled in the relevant art how to both make and use the claimed invention. The instant specification, which provides detailed teachings for producing and using agents to measure βig-h3 levels in urine (see e.g. pages 14-22 of the specification) as well as data in human patients and animals models indicative of increased βig-h3 levels in urine being an indicator of damage to the kidney at an early stage (see Example 4) and predictive of renal disease, clearly meets this requirement.

Withdrawal of this rejection under 35 U.S.C. 112, first paragraph is therefore respectfully requested.

IV. Rejection of Claims 33-38 and 40-43 under 35 U.S.C. 112, second paragraph

Claims 33-38 and 40-43 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner suggests that the phrase "at an early stage" is indefinite because the term "early" is not defined in the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The Examiner also suggests that there is insufficient antecedent basis for the term "the reactant" in parts (b) and (c) of claim 36.

Further claims 36-38 are suggested to be incomplete for omitting essential steps. Specifically, claim 36 only recites a recombinant protein that is contacted with the sample and omits the element of a primary anti-βig-h3 antibody.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended claim 36

to provide for antecedent basis for the term "the reactant" and to include the element of the antibody.

Further, while Applicants believe what is meant by "early stage" renal disease is well known by the skilled artisan and clear when read in light of teachings in the specification, thus meeting the requirements of definiteness as set forth in MPEP 2173.03, in an earnest effort to advance the prosecution of this case, Applicants have amended claims 33 and 40 to recite renal disease at an early stage prior to showing clinical troubles. Support for this amendment is set forth in the specification at page 24, lines 4-9.

Withdrawal of this rejection is therefore respectfully requested.

V. Rejection of Claims 40-43 under 35 U.S.C. 103(a)

Claims 40-43 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Harlow Lane (Antibodies: A Laboratory Manual (1988) Cold Spring Laboratory Press, Cold Spring Harbor, NY, pages 558-559, 570-576, 586-589 and 591-593) in view of Gilbert et al. (Kidney International 54 (1998), 1052-1062) and Zuk et al. (U.S. Patent 4,208,479), or in the alternative as being unpatentable over Harlow & Lane in view of Gilbert et al., Zuk et al. and Ratti et al.

(U.S. Patent 5,629,167). The Examiner suggests that it would have been obvious to one of ordinary skill in the art to employ the competition assay format of Harlow & Lane, which involves providing a sample of the protein to be detected, in order to detect βig-h3 because Gilbert et al. teach that this protein is an index of TGF-β1 bioactivity in the kidney. It would have been further obvious to package all of the reagents necessary (i.e. sample of the βig-h3 protein and an antibody therefor) for performing such an assay into a kit as taught by Zuk et al. for convenience.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended claim 40 to recite a kit for detecting damage to kidneys diagnostic of renal disease at an early stage, comprising a recombinant protein of βig-h3 fas-1 domain consisting of 1 to 10 linked 4th fas-1 domains encoded by SEQ ID NO:6, and an antibody against the recombinant protein of βig-h3 fas-1 domain. Support for this amendment is provided in claim 43. Claims 42 and 43 have been canceled in light of this amendment and claim 44 has been amended to depend from claim 40. As neither of the cited combinations of references teach a recombinant protein of βig-h3 fas-1 domain consisting of 1 to 10 linked 4th fas-1 domains encoded by SEQ ID NO:6, nor

an antibody thereto, the cited combination of references cannot render obvious the instant claimed invention.

Withdrawal of this rejection under 35 U.S.C. 103(a) is therefore respectfully requested.

VI. Conclusion

Applicants believe that this submission comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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